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MESSAGE: Attached is a Reply Brief in response to Examiner's Answer dated November 10, 2003.

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CERTIFICATE OF TRANSMISSION BY FACSIMILE (37 CFR 1.8) Applicant(s): Anderson et al.			Docket No. RU-0115
Serial No. 09/744,002	Filing Date August 2, 2001	Examiner J. Fredman	Group Art Unit 1634

Invention: LINKING GENE SEQUENCE TO GENE FUNCTION BY THREE DIMENSIONAL (3-D) PROTEIN STRUCTURE DETERMINATION

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No.:	RU-0115
Inventors:	Anderson and Montelione
Serial No.:	09/744,002
Filing Date:	August 2, 2001
Examiner:	J. Fredman
Group Art Unit:	1634
Title:	Linking Gene Structure to Gene Function by Three Dimensional (3D) Protein Structure Determination

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On December 31, 2003

Jane Massey Licata Registration No. 32,257

Assistant Commissioner for Patents
Washington, DC 20231

Dear Sir:

REPLY BRIEF

This reply brief is being filed in response to the Examiner's Answer dated November 10, 2003 to address certain issues raised in the Examiner's Answer.

The claimed invention is a method for elucidating the function of proteins and protein domains by examination of their three dimensional structure, and more specifically by the use of bioinformatics, molecular biology and nuclear magnetic resonance spectroscopy to enable the rapid and automated determination of functions, as a means for genome analysis. In this method, the first step of the instant method involves identifying a putative polypeptide domain that properly folds into a stable polypeptide domain having a defined three dimensional structure. This identification step involving a domain is taught at pages 11-18 and Figure 1 of the specification as filed. In the second step of the claimed method, the three dimensional structure of the stable polypeptide domain is then determined. Methods for determining the three dimensional structure of the stable polypeptide domain are taught at pages 3-5 and pages 24-25, and include the preferred method NOESY-Assign process, as well as other methods for analysis of NMR data. The next step involves comparing the determined three dimensional structure of the stable polypeptide domain to known three dimensional structures in a protein data bank in order to identify known structures within the protein data bank that may be homologous to the

determined three dimensional structure. This step in the method is discussed at page 26. The final step in the claimed method involves correlating a biochemical function corresponding to the identified homologous structure to a biochemical function for the stable polypeptide domain. This part of the method is described at pages 26-28. Further, the method of the present invention is shown graphically as a flow chart in Figure 1.

Appellants respectfully disagree with the reasoning set forth by the Examiner as the basis for not granting priority to the parent application Serial No. 09/181,601 in the Answer dated November 10, 2003. Contrary to the Examiner's suggestion, Appellants have complied with MPEP § 201.08 which states that a continuation-in-part may be filed during the lifetime of an earlier nonprovisional application, repeating some substantial portion or all of the earlier nonprovisional application and *adding matter not disclosed* in the said earlier nonprovisional application.

As described in detail in the main Appeal Brief, the claim limitation of "NOESY-assign process" may claim priority back to the parent case as it is a preferred method of determining the three dimensional structure of a stable polypeptide domain. By analogy there are many means of determining the size of a protein (*e.g.*, HPLC, PAGE, etc.) and the skilled artisan would not need to have provided to him/her a detailed list of each and every

means to understand that certain methods may be better than others. If, however, a preferred HPLC column type, for example, which was not mentioned in a parent application were found to be more amenable to separating a protein based on that particular protein's structural/function characteristics it would be appropriate subject matter for a continuation-in-part application. For example, U.S. Patent No. 5,391,706 claims a method of purifying GM-CSF wherein the fourth step of the purification process utilizes a Red 102 triazinyl dye-ligand affinity column; however, nowhere in the parent application WO 89/00579 is there any mention of a Red 102 triazinyl dye affinity column.

Appellants also respectfully disagree with several points of reasoning set forth by the Examiner as the basis for maintaining the rejection under 35 U.S.C. § 103 in the Answer dated November 10, 2003. Appellants believe that the Examiner has mischaracterized the teachings of Wallace et al. as it applies to the teachings of the claimed invention as whole. Specifically, at pages 17-19 of the Examiner's Answer, it is suggested that Wallace et al. teach the analysis of entire protein sequences which are of greater than 50 amino acids to determine the three amino acids involved in the actual catalysis and that the three amino acids in the context of the folds and three dimensional

structure and context provided by all the remaining amino acids in the protein must be considered.

However, the pending claims are expressly limited to protein domains of preferably 50 to 300 amino acids in length. As is well-known in the art, a protein domain is a region within a protein that has been distinguished by a well-defined set of properties or characteristics. In general, a protein domain is less than the entire protein sequence and in the case of Wallace et al., the domain is comprised of three amino acids which are brought into close proximity by the entire protein structure. Thus, unlike Wallace et al., the instant invention relates to determining the function of proteins and protein domains by examining the three dimensional structure of structural domains wherein the entire protein sequence need not be utilized and the domains are preferably 50 to 300 amino acids in length.

Wallace et al. teach and expressly demonstrate via the protein structures depicted in the figures that entire protein sequences were used in the determination of catalytic triad domain consisting of three amino acids. Thus, upon reading the teachings of Wallace et al. it would not be obvious to one of skill in the art that a domain of preferably 50 to 300 amino acids that properly folds into a stable polypeptide domain could be extracted from an unknown protein and be used in determining three dimensional structure and subsequent function of the

unknown protein. First Wallace et al. teach the use of the entire protein sequence of known proteins to determine the three amino acid domain which comprises the catalytic triad. Second, Wallace et al. then use the Ser-His-Asp catalytic triad domain template with an RMS distance cutoff of 2.0 Å to identify other proteins with triplets that lie within the constraints of this template. Thus, Wallace et al. do not teach success in using domains of preferably 50 to 300 amino acids in determining the biochemical function of a protein or polypeptide domain of unknown three dimensional structure and function.

The prior art of Wallace et al. in combination with the secondary references, when viewed as whole, simply do not provide the requisite teaching or suggestion to render the claimed invention, when viewed as a whole, obvious.

Respectfully submitted,

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DATE: December 31, 2003

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